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# Residual Ethylene Oxide in Gas-Sterilized Medical-Grade Silicones

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**Abstract** □ Residual gas was extracted from ethylene oxide-treated silicone sheets by high vacuum distillation, and the residue subsequently was analyzed by GLC. To indicate the necessary aeration time of the materials before they can be considered safe to use, the desorption characteristics of ethylene oxide in three types of the silicone polymer were studied. Very rapid desorption of the gas to low residual levels was observed in the two nonreinforced silicone rubbers examined: medical-grade silicone sheeting and a medical-grade elastomer. The third material, Dacron-reinforced silicone sheeting, lost the gas at a considerably slower rate, after an initial rapid drop, due to retention by the Dacron reinforcement.

**Keyphrases** □ Silicone sheets, medical grade—absorption and diffusion of ethylene oxide after gas sterilization □ Ethylene oxide gas sterilization—absorption and diffusion from medical-grade silicone sheets □ Sterilization with ethylene oxide —absorption and diffusion from medical-grade silicone sheets

During the last couple of decades, there has been an ever increasing trend to utilize synthetic rubber and plastics in medical instruments and equipment as well as in permanent or semipermanent implants and prostheses. Because many synthetic materials are heat labile, conventional dry heat or autoclaving processes have been substituted by low temperature sterilization methods.

One such method is ethylene oxide gaseous sterilization, and its relative merits have already been well documented. However, one serious disadvantage of sterilization with this gas is that ethylene oxide remains in the material, and its presence in a polymeric device can present potential toxicological problems if the gas is released to tissue. Only in recent years, with the increasing use of GLC, has it been discovered that various types of polymeric materials may contain reaction products of ethylene oxide other than ethylene glycol, such as the highly toxic ethylene chlorohydrin (2-chloro-

ethanol) which is formed in the presence of chloride ions (1, 2).

Medical-grade silicones are widely used in tissue implants and can be successfully sterilized both by conventional methods and by ethylene oxide. With the latter method, there is uncertainty concerning the retention time of the gas, together with the possibility of cytotoxic reaction products. These considerations prompted this study.

## THEORY

If there is a uniform distribution of a dissolved gas in a thin slab of material and the surfaces are suddenly exposed to zero partial pressure of the gas and maintained at that, the gas begins to clear from the material. It can be shown (3) that, after an initial period during which the mean gas concentration in the medium decreases by 10-20%, the concentration at all points decreases exponentially with the same half-time:

$$T_{1/2} = \frac{2.77 \left( \frac{L}{2} \right)^2}{\pi^2 D} \quad (\text{Eq. 1})$$

where:

$T_{1/2}$  = half-time (sec.)

$L$  = thickness of material (cm.)

$D$  = diffusion coefficient (cm.<sup>2</sup>sec.<sup>-1</sup>)—constant for a given gas, temperature, and material

Thus, if the total amount of dissolved gas can be calculated as a function of time, the diffusion coefficient can be deduced from the slope of the exponential (which indicates the time taken for the concentration of dissolved gas to decrease by half) and the thickness of the medium; repeating the experiment with a different thickness of the material provides a check on the value.

The  $T_{1/2}$  of Eq. 1 is also a measure of the rate of diffusion into the material.

Table I shows the diffusion coefficient of ethylene oxide in several plastics at 23°. Knowledge of the diffusion coefficient of ethylene oxide in a particular material at room temperature should permit

**Table I**—Diffusion Coefficient of Ethylene Oxide in Polyethylene, Polypropylene, and Polybutylene at 23°<sup>a</sup>

Polymer	Density, g. cm. <sup>-3</sup>	Diffusion Coefficient, cm. <sup>2</sup> sec. <sup>-1</sup>
Polyethylene	0.913	$6.17 \times 10^{-8}$
Polyethylene	0.917	$3.52 \times 10^{-8}$
Polyethylene	0.930	$1.83 \times 10^{-8}$
Polyethylene	0.963	$1.30 \times 10^{-8}$
Polypropylene	0.904	$0.44 \times 10^{-8}$
Polypropylene	0.906	$1.09 \times 10^{-8}$
Polybutylene	0.914	$1.09 \times 10^{-8}$

<sup>a</sup> From data shown in Table X of Reference 4.

some predictions to be made concerning the minimum aeration time necessary to achieve sterile, nontoxic medical devices manufactured from that material.

### EXPERIMENTAL

**Materials**—Medical-grade silicone sheeting<sup>1</sup>, reinforced and nonreinforced, and a room temperature vulcanizing medical-grade silicone elastomer (Silastic 382)<sup>1</sup> were used.

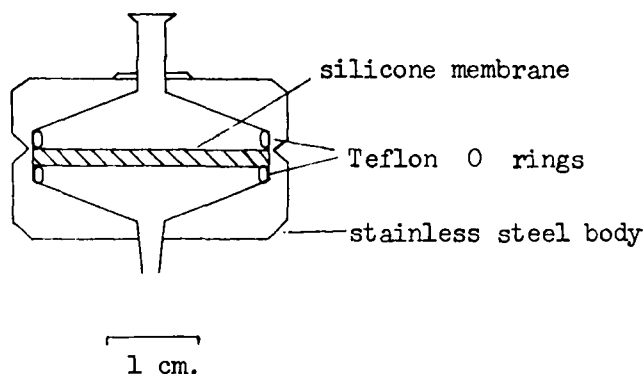
**GLC**—A dual flame-ionization gas chromatograph<sup>2</sup> was used. The columns were of glass tubing, 4 mm. i.d. and 1.5 m. (5 ft.) in length. The packing consisted of 80-100-mesh Porapak Q<sup>3</sup> for the estimation of ethylene oxide and of polyethylene glycol 20,000, 10% w/w, on 100-120-mesh Diatomite C<sup>3</sup> for the estimation of ethylene chlorohydrin. Nitrogen was used as the carrier gas at a flow rate of 45 ml. min.<sup>-1</sup> with a column oven temperature of 125°, an injection temperature of 175°, and a detector oven temperature of 200°. The injection solvent was distilled water. Peak areas were obtained from the product of the peak height and the width at half the peak height.

**IR Determinations**—A double-beam grating IR spectrophotometer<sup>4</sup> was employed. Standard gas cells (150-ml. capacity) were used to follow the uptake of ethylene oxide by the silicone, with measurements being made at 11.5 μ. Internal reflection spectroscopy was carried out using a KRS-5 crystal (thallous-bromide-iodide complex)<sup>5</sup> and a beam incidence angle of 60°.

**Exposure to Ethylene Oxide**—Uniformly thin sheets of the three types of silicone were cut into strips (each measuring approximately 20 × 76 mm.), which were freely suspended from a glass rod by metal clips. The strips of the different materials were then exposed in turn to pure ethylene oxide (1200 mg. l.<sup>-1</sup>) at 23° and 60% relative humidity in the gas sterilizer<sup>6</sup> for a sufficient time to ensure equilibration (24 hr.). Three manual evacuation cycles were then carried out to empty the sterilizer chamber of the toxic ethylene oxide, and the strips were removed from the sterilizer. This procedure was followed by aeration at 23° under a gentle stream of air, the samples being taken at accurately timed intervals for extraction and analysis.

**Extraction of Residual Ethylene Oxide**—Vacuum extraction techniques for residual ethylene oxide and its reaction products have already been used successfully (5-7). The method employed here was based on distillation under high vacuum, with a distillate trap cooled in liquid nitrogen. The extracted sterilant residues were then dissolved in a small volume of distilled water for quantitative determination by GLC.

**Diffusion Cell**—A small, stainless steel diffusion cell was set up using a filter<sup>6</sup>, with the silicone as a membrane to form the two compartments of the cell (Fig. 1). A 50-ml. gas syringe full of pure ethylene oxide was attached to one side while an empty syringe, equipped with a sampling device, was fitted to the other compartment; the pistons of the syringes allowed the contained gases to remain at atmospheric pressure at all times. The system was tested underwater for leaks and found to be gas tight. Samples were withdrawn at timed intervals from the receiver compartment and estimated on the gas chromatograph.



**Figure 1**—Diffusion cell (25-mm. diameter microsyringe filter holder).

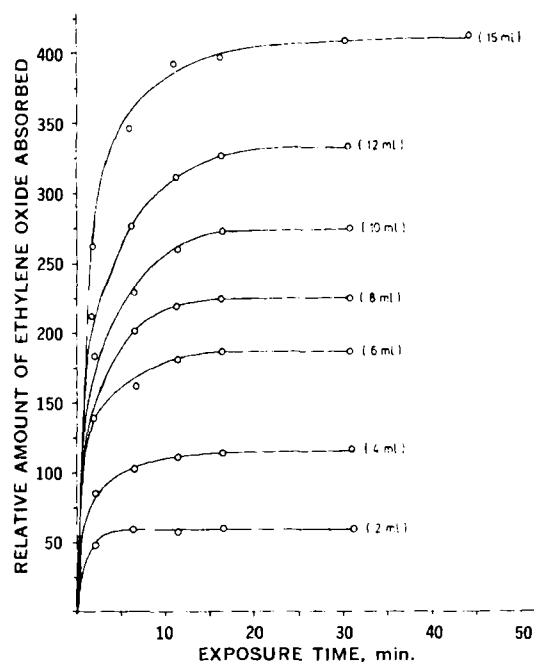
### RESULTS AND DISCUSSION

The results obtained for the uptake of ethylene oxide by the heat vulcanized silicone using the IR spectroscopy method and measuring the decrease in absorbance at 11.5 μ are displayed in Fig. 2. It can be seen that equilibration occurs within a short time.

By plotting the logarithm of residual ethylene oxide versus desorption time, the predicted straight-line graphs of Fig. 3 are obtained; these plots permit ready calculation of the diffusion coefficient of ethylene oxide in the elastomer, a room temperature vulcanized silicone rubber.

The desorption curves of ethylene oxide from heat vulcanized silicone sheeting, nonreinforced and Dacron reinforced (Figs. 4 and 5, respectively), suggest a two-stage desorption mechanism and require further investigation. An examination of Fig. 4 showed that it was possible that a compressed film of ethylene oxide had built up on the surface of the heat vulcanized silicone without gas penetration into its interior. Removal from the sterilizer would produce rapid loss of this surface film until only a relatively strongly held monolayer of adsorbed ethylene oxide remained. (This would correspond to the almost horizontal part of the curves and the amount agrees closely with calculation of monolayer capacity.)

This possibility was investigated in two ways:



**Figure 2**—Plot of amount of ethylene oxide absorbed in 1.0-mm. thick, heat vulcanized silicone rubber versus time exposed to the gas. The volume of ethylene oxide admitted to the gas cell is shown in parentheses beside each curve.

<sup>1</sup> Dow Corning Center for Aid to Medical Research, Midland, Mich.

<sup>2</sup> Pye Series 104.

<sup>3</sup> Pye Unicam, Cambridge, England.

<sup>4</sup> Perkin-Elmer 237.

<sup>5</sup> "Victoria Steriliser," The Medical Supply Association Ltd., London, England.

<sup>6</sup> Millipore, Millipore Corp., Bedford, Mass.

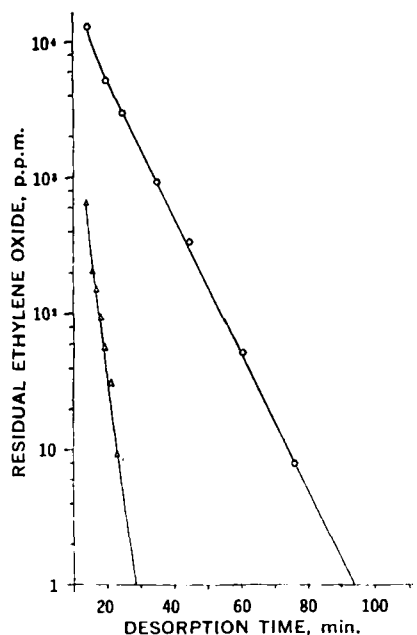


Figure 3—Plot of log residual ethylene oxide in room temperature vulcanized silicone elastomer versus desorption time. Key: O, 2.0-mm. thick sheet; and  $\Delta$ , 1.0-mm. thick sheet.

1. By internal reflection spectroscopy, an IR technique used essentially to study surface phenomena. This technique was employed in an effort to detect the existence of a thin film of adsorbed ethylene oxide on the silicone immediately after removal from the sterilizer. No ethylene oxide was detected; however, this does not exclude the possibility of a monomolecular surface layer because the sensitivity of the method is low.

2. By determining the diffusion of ethylene oxide through a membrane of the silicone in the diffusion cell. The results (Fig. 6) indicate that ethylene oxide is, in fact, absorbed by heat vulcanized silicone and diffuses very rapidly through it. With this knowledge, the shape of the desorption curves of Fig. 5 can be explained by the relatively slow release of absorbed ethylene oxide from the Dacron tricot weave reinforcement in the middle of the sheet of heat vulcanized silicone.

Since it had been confirmed that absorption and diffusion do occur, the diffusion coefficient of ethylene oxide in the two non-

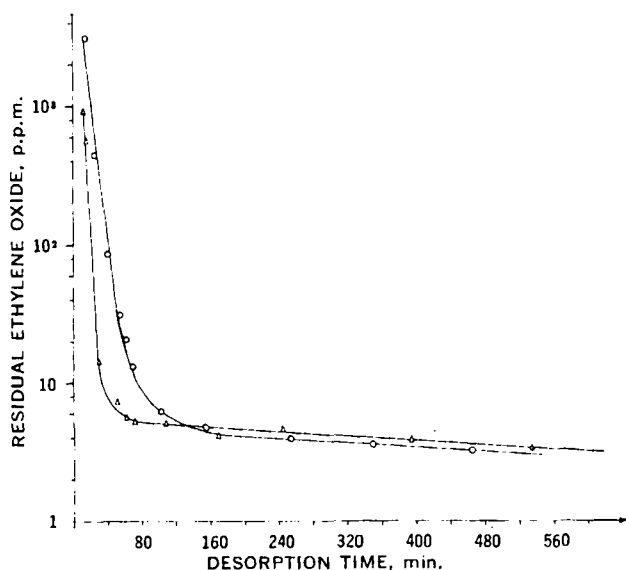


Figure 4—Plot of log residual ethylene oxide in heat vulcanized silicone rubber versus desorption time. Key: O, 1.6-mm. thick sheet; and  $\Delta$ , 1.0-mm. thick sheet.

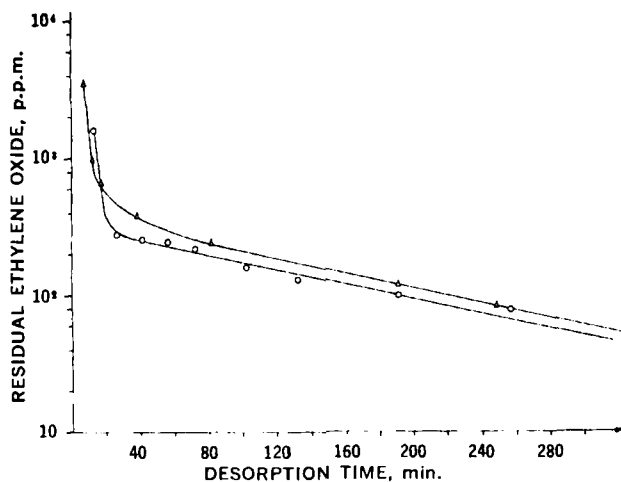


Figure 5—Plot of log residual ethylene oxide in Dacron-reinforced heat vulcanized silicone rubber versus desorption time. Key: O, 1.0-mm. thick sheet, and  $\Delta$ , 0.76-mm. thick sheet.

reinforced materials was calculated using Eq. 1; the results are shown in Table II.

Since Fig. 5 indicates that it is the Dacron reinforcement and not the silicone that governs the desorption of ethylene oxide, it was not possible to obtain a value for the diffusion coefficient of the gas in the reinforced material. However, it was noted that during the first 45 min. after removal from the sterilizer the ethylene oxide level dropped to approximately 10% of its equilibrium value; thereafter, the half-time (*i.e.*, the time for the concentration of dissolved ethylene oxide to decrease by half) was observed to be about 100 min., which would seem to imply that reinforced silicone sheeting is completely safe to use after 24 hr. aeration.

Although the vacuum process is known to extract reaction products of ethylene oxide when these are present (and has been successfully used for this purpose by the authors), none was detected in any silicone sheeting.

An incontinence implant was used as the test piece in the final

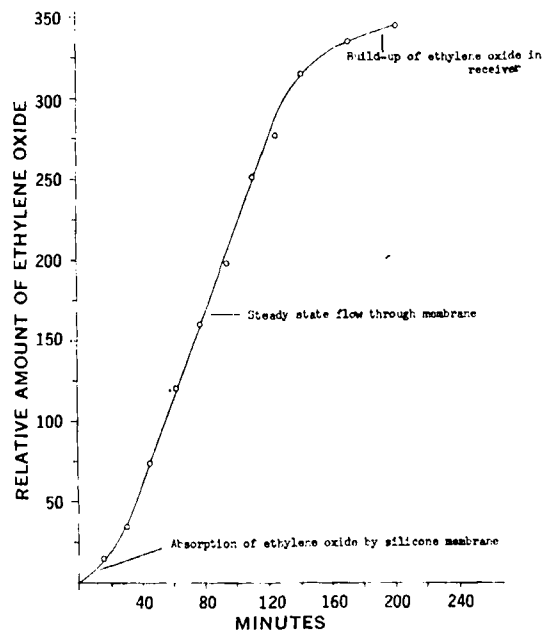


Figure 6—Plot of amount of ethylene oxide which has diffused through a 1.0-mm. thick membrane of heat vulcanized silicone rubber versus time.

**Table II—Diffusion Coefficient of Ethylene Oxide in Silicone Sheeting at 23°**

Material	Mean Thickness, mm.	Diffusion Coefficient, cm. <sup>2</sup> sec. <sup>-1</sup>
Room temperature vulcanized silicone	1.0	$7.7 \times 10^{-6}$
	2.0	$8.0 \times 10^{-6}$
Heat vulcanized silicone sheeting	1.0	$4.3 \times 10^{-6}$
	1.6	$4.2 \times 10^{-6}$

study to predict minimum aeration time using the diffusion coefficient. The body of the device, comprising the electronic components enclosed in room temperature vulcanized silicone, measured 38 mm. in diameter and was 10.8 mm. deep. Attached to it were two 23 mm. long wire leads, surrounded by heat vulcanized silicone approximately 0.7 mm. thick.

Two assumptions were made in working out the theoretical aeration time for the level of residual ethylene oxide to fall to a low value: (a) the body of the device could be considered as being composed entirely of room temperature vulcanized silicone, and (b) the silicone would contain a maximum of 13,000 p.p.m. ethylene oxide after sterilization. (This value comes from the previous experiments on this material.)

The first assumption is not entirely unjustified since any void areas in the center of the electronics compartment will have attained the equilibrium concentration of ethylene oxide throughout the surrounding silicone. Since the half-time for this thickness of silicone is approximately 170 min. at 23°, after sterilization at 50° for 1 hr. a uniform equilibrium concentration of absorbed ethylene oxide (13,000 p.p.m.) will probably not have been achieved.

Ignoring losses from the sides of the body, the time necessary to fall to 10 p.p.m. ethylene oxide was calculated using Eq. 1 and the experimental value of the diffusion coefficient of ethylene oxide in room temperature vulcanized silicone at 23°; the time was found to be about 27 hr.

This value was tested using the implant device described. The article, wrapped in the routine paper-polypropylene pack which presents no barrier to the passage of ethylene oxide gas, was subjected to the normal sterilizing procedure, i.e., exposure to 1200 mg. ethylene oxide/l. for 1 hr. at 50°, followed by seven automatic evacuation cycles of the chamber. Aeration at the ambient tem-

perature (23°) was for 24 hr., after which the analysis was carried out; 4 p.p.m. ethylene oxide was detected.

## CONCLUSIONS

This study shows that the diffusion of ethylene oxide in non-reinforced medical-grade silicone (heat or room temperature vulcanized) is extremely rapid and that in the case of relatively simple shapes the minimum aeration time required to eliminate ethylene oxide can be obtained from Eq. 1.

Dacron-reinforced silicone sheeting loses the gas at a considerably slower rate due to retention by the Dacron reinforcement, and it is recommended that a minimum aeration of 24 hr. be adopted for this material.

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